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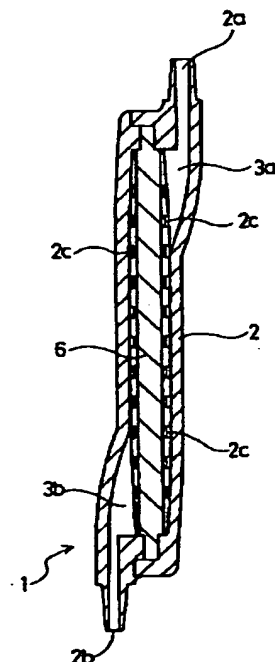
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(54) 【発明の名称】 白血球分離用フィルターおよび白血球除去器

(57) 【要約】

【目的】 白血球または血小板に対して、高くても安定した捕捉能を有し、血液中より短時間に効率よく白血球または血小板を分離することができ、また、操作時における異物の流出のおそれがなく安全で、さらに、製造が容易で、かつ製品の性能のバラツキの少ない白血球分離用フィルター、または白血球および血小板分離用フィルターを提供する。

【構成】 この白血球分離用フィルターは、最頻孔径が1～5 μ mで、かつ、最平均孔径と数平均孔径との比が1.5～2.5である三次元網目状連続多孔体により形成されている。



Original document

LEUKOCYTE SEPARATION FILTER AND LEUKOCYTE REMOVER

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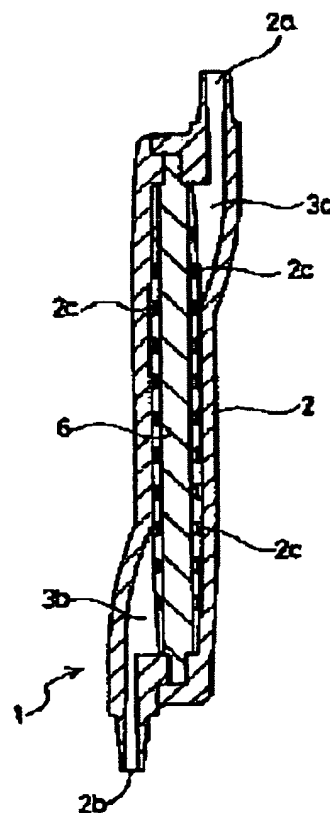


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Abstract of JP7124255

PURPOSE: To prepare a leukocyte separation filter having freedom from a concern about the outflow of a foreign substance at the time of operation and a high and stable collection function for leukocyte by forming the filter out of a three-dimensional mesh type continuous porous body having a specific value as a most frequent hole diameter, and another specific value as a ratio of a quantitative mean hole diameter to a numerical mean hole diameter. **CONSTITUTION:** A leukocyte remover 1 using a leukocyte separation filter 6 is formed out of a housing having a blood inflow port 2a and a blood outflow port 2b, and a leukocyte separation filter 6 laid so as to divide the internal space of the housing 2 into a blood inflow section 3a and a blood outflow section 3b. Also, the filter 6 is formed out of a three-dimensional mesh type continuous porous body having a value between 1 and 5 μm as a most frequent hole diameter, and a value between 1.5 and 2.5 as a ratio of quantitative mean hole diameter to numerical mean hole diameter. The filter 6 so formed has a high and stable collection function for leukocyte, and the leukocyte contained in blood, when passing a complicated flow passage between the matrices of the porous body, is efficiently collected in a short time.

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This invention relates to filters for separating leukocytes, leukocyte removers, filters for separating both leukocytes and platelets, and leukocyte/platelet removers. It is concerned to provide those having an excellent capability for capturing

leukocytes without suffering from contamination with foreign matter.

In recent years, blood transfusion has largely changed from conventional whole blood transfusion to blood component transfusion, in which only a necessary component is transfused to a patient. An important problem in blood component transfusion is how to increase the purity of respective fractionated blood components.

Blood from donors has conventionally been centrifugally separated into concentrated red cells (CRC), a platelet concentrate (PC), and a platelet-poor plasma (PPP). Blood preparations obtained by the separation of blood are used for blood component transfusion to patients who need red cells or platelets. However, since a large amount of leukocytes are contained in blood preparations, problems may sometimes occur if a large amount of leukocytes are introduced into patients by transfusion.

Leukocytes contained in blood preparations must be removed as far as possible for the purpose of avoiding side effects, particularly post-transfusion reactions. To date, a number of improvements have been proposed for this purpose. In some extraction of red cells alone by excluding leukocytes and platelets is also required. Used for these purposes are a method capturing member, a gravitational centrifugal separation method utilizing the difference in specific gravity between blood, a method utilizing the viscosity or adhesion of leukocytes, etc.

Among them, the method using a capturing member is widely used because of good efficiency in removing leukocytes or leukocytes and platelets, easiness of handling, etc. Capture members often used are fibers having extremely small diameters such as natural fibers, synthetic fibers, etc. packed into a column, or non-woven fabrics formed by secondarily processing

The use of such fibers, however, is likely to suffer from detachment of some fibers or outflow of foreign matters during operation. If the fiber packing density is increased for the purpose of sufficiently capturing leukocytes or platelets, trapped cells tend to clog pores between the fibers.

On the other hand, there are various proposals to use porous members as the capturing members. For example, Japanese Publication No. 61-39060 discloses the use of a porous member including continuous fine pores with an average pore diameter of 25 μm to 60 μm to capture highly viscous monocytes and granulocytes. Japanese Patent Publication No. 63-2608 discloses a method using a porous member having continuous pores with an average pore diameter of 5 μm to 20 μm to capture leukocytes by utilizing the viscosity of white cells and by filtration with the fine pores of the porous members.

However, in view of the recent demand for more effective removal of leukocytes, the above porous members having relatively large pore diameters do not provide satisfactory leukocyte separation. Leukocyte-separating abilities are elevated by reducing the pore diameter (for example, by reducing the average pore diameter to less than μm or so); however, blood cells tend to clog the pores of the porous members, taking much time for filtration.

Thus, there have so far been no leukocyte filters, leukocyte/platelet-separating filters, and removers comprising such filters with sufficient performance for the practical purpose, and their improvements are still desired.

It is therefore an object of the present invention to provide a leukocyte-separating or leukocyte/platelet filter suffering from no outflow of foreign matters during operation, having a high and stable capability of capturing leukocytes, and capable of efficiently and quickly separating leukocytes, or leukocytes and platelets, from blood or blood preparations.

Another object of the present invention is to provide a leukocyte or leukocyte/platelet remover comprising such a filter.

The first filter according to the present invention comprises a three-dimensionally reticular, porous member with continuous open pores having a most frequent pore diameter in the range of 1 μm to 5 μm and a ratio of a weight-average pore diameter to a number-average pore diameter in the range of 1.5 to 2.5.

A leukocyte/platelet-separating filter embodying the present invention comprises a laminate of at least one platelet-nonadsorbing, three-dimensionally reticular, porous member with continuous open pores having a most frequent pore diameter in the range of 1 μm to 5 μm and a ratio of a weight-average pore diameter to a number-average pore diameter in the range of 1.5 to 2.5, and at least one platelet-adsorbing, three-dimensionally reticular, porous member with continuous open pores having a most frequent pore diameter in the range of 1 μm to 5 μm and a ratio of a weight-average pore diameter to a number-average pore diameter in the range of 1.5 to 2.5.

A leukocyte remover embodying the present invention comprises a housing having a blood inlet and a blood outlet; and a filter laminate as defined above disposed in the housing such that it partitions the interior of the housing into a blood inlet portion and a blood outlet portion.

In the drawings:

Fig. 1 is front elevational view showing a leukocyte remover including a leukocyte-separating filter according to an embodiment of the present invention;

Fig. 2 is a right side elevational view of Fig. 1;

Fig. 3 is a cross-sectional view taken along the A-A line in Fig. 1;

Fig. 4 is a front elevational view showing a leukocyte/platelet remover including a leukocyte/platelet-separating filter according to an embodiment of the present invention;

Fig. 5 is a right side elevational view of Fig. 4;

Fig. 6 is a cross-sectional view taken along the B-B line in Fig. 4;

Fig. 7 is a schematic view showing a circuit including the leukocyte-separating filter according to the present invention;

Fig. 8 is a schematic view showing another circuit including the leukocyte-separating filter according to the present invention;

Fig. 9 is a schematic view showing a circuit including the leukocyte/platelet-separating filter according to the present invention;

Fig. 10 is a schematic view showing another circuit including the leukocyte/platelet-separating filter according to the present invention; and

Fig. 11 is a schematic view showing an experimental circuit with a leukocyte-separating filter used in Examples and Comparative Examples.

Embodiments of the present invention will be described below in detail.

[1] Leukocyte-separating filter

A leukocyte-separating filter explained in this Section is one for separating leukocytes alone. A filter for separating both leukocytes and platelets will be explained in Section [2].

The leukocyte-separating filter is composed of a three-dimensionally reticular, porous member having continuous open pores whose most frequent pore diameter is 1 μm to 5 μm . If the most frequent pore diameter is smaller than 1 μm , other cells contained in blood or a leukocyte suspension to be treated are also captured during leukocyte removal operation, possibly clogging the filter. On the other hand, if the most frequent pore diameter is larger than 5 μm , the frequency of contact with leukocyte suspension to be treated is lowered, possibly decreasing the blood cell capturing rate. The more preferable most frequent pore diameter of the leukocyte-separating filter is 2 μm to 4 μm .

The term "most frequent pore diameter" used herein means a pore diameter which the largest number of pores have, and defined as a most frequently occurring diameter (peak value) in a distribution of pore diameters. The pore diameter distribution is obtained by cutting a porous member along an arbitrary surface, measuring cross section areas of respective pores distributed throughout the entirety of the cross section surface, calculating diameters of the pores assuming that they are converted into circular pores, and plotting the pore diameters on a graph in which the abscissa indicates pore diameters at 1- μm intervals and the ordinate indicates the number of pores in every interval (every 1 μm). Thus, the most frequent pore diameter is a pore diameter most often shown, regarding all of the pores having variable shapes and diameters as circular cross-sectional pores. In order to ensure a reliability, not less than 2000 pores are preferably measured at random.

By the foregoing definition, the most frequent pore diameter does not necessarily represent the largest diameter among the existing pores, but merely means that the number of pores having larger or smaller diameters than the most frequent pore diameter gradually decreases. Therefore, the most frequent pore diameter does not even mean that particles having larger diameters do not pass through the porous member. Although red cells in general have larger diameters than the most frequent pore diameter, living red cells can freely deform and pass through the pores.

The porous member constituting the leukocyte-separating filter is characterized by having an average pore diameter ratio (of a weight-average pore diameter to a number-average pore diameter) of 1.5 to 2.5. If the average pore diameter ratio is less than 1.5, clogging is liable to occur, and filtration takes much time. If it exceeds 2.5, the capturing rate is liable to decrease.

The weight-average pore diameter is a value defined by $\text{SIGMA } R_i^2 / \text{SIGMA } R_i N_i$ similarly to the equation of the average molecular weight, and the number-average pore diameter is a value defined by $\text{SIGMA } R_i N_i / \text{SIGMA } N_i$, where R_i is the pore diameter measured by a mercury infiltration method, and N_i is the number of pores having a diameter R_i . The pore diameter R_i is determined by randomly cutting a porous member, measuring cross section areas of respective pores distributed throughout the entirety of the cross section surface, converting the cross sections of the pores to circles, and calculating diameters of the circles. As explained above, the average pore diameter ratio represents a distribution of pore diameters. The larger the value of the average pore diameter ratio, the wider the distribution of pore diameters, meaning that there are many pores having larger diameters than the most frequent pore diameter and many pores having smaller diameters than the most frequent pore diameter.

The porosity of a platelet-nonadsorbing, three-dimensionally reticular, porous member with continuous open pores is preferably 75% to 95% and more preferably 80% to 95%, although it may vary depending on the most frequent pore diameter, etc. If the porosity is 75% or more, leukocytes are removed in a short time. If the porosity is 95% or less, a sufficient strength for a filter is obtained. The thickness of the porous member is preferably 0.1 mm to 10 mm and more preferably about 0.5 to 3 mm, although it may vary depending on the most frequent pore diameter, porosity and microstructure of the porous member. If the porous member is 0.1 mm or thicker, the filter is strong enough. On the other hand, if it is 10 mm or thinner, the length of filtration path is not excessive, and clogging is unlikely to occur.

The leukocyte-separating filter may be composed either of a single porous member in the form of a flat sheet or of a plurality of such porous members. Preferably, however, a plurality of flat porous members are stacked to provide a laminate. In case the leukocyte-separating filter is composed of a plurality of porous members, it is preferred to dispose one or more porous members having wider pore diameter distributions (larger average pore diameter ratios) on the upstream side and one or more porous members having narrower pore diameter distributions (smaller average pore diameter ratios) on the downstream side. Placing the porous member having a wider pore diameter distribution on the upstream side provides efficient separation of leukocytes without increasing filtration resistance.

The three-dimensionally reticular, porous member with continuous open pores constituting the leukocyte-separating filter having the above characteristics is made of a platelet-nonadsorbing material. The term "platelet-nonadsorbing" used here means a characteristic of adsorbing substantially no platelet, and does not necessarily mean absolute non-adsorption of platelets. Preferable materials therefor are ethylene-vinyl alcohol copolymers, polyurethanes of any types including a polyether type, polyester type and a polycarbonate type (preferably polyurethanes containing polyethers such as polytetramethylene oxide, polypropylene oxide or polyethylene oxide), fluorocarbon polymers (preferably polyvinylidene fluoride), polysulfones, and polyether sulfones. Particularly preferable are polyurethanes.

A preferable method for manufacturing the porous member is a so-called elution method which comprises extruding a film made of a resin composition including a polymer such as polyurethane, polyvinylidene fluoride, polysulfone, polyester, polyamide, etc., a good solvent therefor and a pore-creating agent soluble in or swellable with a non-solvent having a compatibility with the good solvent, and then immersing the extruded flat sheet in the non-solvent to cause gelation while eluting out the pore-creating agent, thereby forming a flat porous sheet or film having "through-pores," pores penetrating one side to the other of the porous sheet or film. A preferable ratio of the polymer in the resin composition is 5 weight % to 95 weight %. Preferable good solvents are dimethyl formamide, dimethyl sulfoxide, acetone, dioxane, methyl Cellosolve acetate, tetrahydrofuran, ethyl alcohol, methyl alcohol, methyl ethyl ketone, etc. Preferable pore-creating agents are polyvinyl alcohol, polyvinyl pyrrolidone, methyl cellulose, polyether, polysaccharide, polyacrylic acid, etc. A preferable amount of the pore-creating agent added is 5 weight % to 50 weight % based on the composition to provide the porous member with continuous open pores (fine through-pores). This manufacturing method is described in detail in Japanese Patent Laid-open No. 3-47,342 in the case of polyurethane, it may be coated on another material.

Since the leukocyte-separating filter of the present invention exhibits a high and stable capability of capturing leukocytes efficiently and quickly separate leukocytes from a platelet concentrate (PC), concentrated red cells (CRC) or a whole blood without danger of outflow of foreign matters during operation. Further, the leukocyte-separating filter suffers from little loss in performance.

[2] Filter for Separating Leukocytes and Platelets

A filter for separating leukocytes and platelets (leukocyte/platelet-separating filter) may be either composed of one or more platelet-adsorbing, three-dimensionally reticular, porous member with continuous open pores, or of a laminate of one or more platelet-nonadsorbing, three-dimensionally reticular, porous members with continuous open pores and one or more platelet-adsorbing, three-dimensionally reticular, porous members with continuous open pores. In any case, the porous members have a most frequent pore diameter of 1 μm to 5 μm and an average pore diameter ratio (ratio of a weight-average pore diameter to a number-average pore diameter) of 1.5 to 2.5 in order to have a good leukocyte-separating capability. For the same reasons stated above, the most frequent pore diameter is preferably 2 μm to 4 μm .

The platelet-nonadsorbing, three-dimensionally reticular, porous member with continuous open pores may be the same as explained in [1] above. In contrast, the platelet-adsorbing, three-dimensionally reticular, porous member with continuous open pores may be made either of a platelet-adsorbing material or of a cationic-treated platelet-nonadsorbing or platelet-adsorbing material.

Platelet-adsorbing materials usable in the present invention are polyvinyl acetals (preferably polyvinyl formal), aliphatic polyamides which may be nylon 6, nylon 66, nylon 12, or so-called polyetheramides copolymerized with polyether compounds such as polytetramethylene oxide, polypropylene oxide and polyethylene oxide, aromatic polyamides (preferably, in particular polymethaphenylene isophthalic amide or polyparaphenylene terephthalic amide), polyesters (in particular polybutylene terephthalate, polyethylene terephthalate, etc.), polyimides, etc.

The term "cationic treatment" used herein means to adhere or bond a cationic compound to a surface of a filter substrate or to incorporate the cationic compound into the filter substrate. Specifically, there are methods of coating the porous member with a cationic compound, methods of bonding the cationic compound to the filter substrate by grafting copolymerization, etc., methods of mixing the filter substrate with the cationic compound in the process of fabrication of the porous member. Cationic compounds usable are quaternary ammonium salts, compounds having amino groups or imino groups, etc. For example, a preferable method for bonding the cationic compound to the filter substrate by graft copolymerization, the filter substrate is subjected to a plasma treatment, and graft-copolymerized with a monomer having a reactive substituent such as glycidyl methacrylate, and then a cationic agent is bonded to the grafted monomer. Cationic treatment contributes to maintaining a positive charge of the filter for a long period of time.

The platelet-adsorbing, three-dimensionally reticular, porous member with continuous open pores has a porosity of 75% and a thickness of 0.1 mm to 10 mm for the reason described in [1] above.

The platelet-adsorbing, three-dimensionally reticular, porous member with continuous open pores may be produced by a method, provided that the porous member has the aforementioned structure. A preferable method is an elution method. In case of making the porous member of polyvinyl formal, for example, the elution method uses an acetal-forming reaction which formaldehyde and an acid catalyst acts on an aqueous polyvinyl alcohol solution containing a pore-creating agent from amylose-containing polysaccharide such as starch and dextrin, derivatives thereof, acid-proof anionic surfactants, r surfactants, etc. optionally in the presence of an inorganic salt such as sodium sulfate, sodium chloride, ammonium sulfate, ammonium chloride, potassium sulfate, sodium iodide, etc. (Patent Publication Nos. 47-46455 and 48-20019).

With a high and stable capability of capturing leukocytes and platelets, the leukocyte/platelet-separating filter of the present invention can efficiently and quickly separate leukocytes and platelets from concentrated red cells (CRC) and a whole blood without danger of outflow of foreign matters during operation. It also reduces variance in performance.

[3] Leukocyte Remover

A leukocyte remover equipped with the leukocyte-separating filter according to the present invention will be explained in detail with reference to Figs. 1 to 3. Fig. 1 is a front elevational view of an example of the leukocyte remover with the leukocyte-separating filter according to the present invention, Fig. 2 is a right side elevational view of Fig. 1, and Fig. 3 is a cross-sectional view taken along the A-A line in Fig. 1.

The leukocyte remover 1 with the leukocyte-separating filter 6 according to the present invention is composed of a housing 2 having blood inlet 2a and a blood outlet 2b, and a leukocyte-separating filter 6 constituted by a three-dimensionally reticular porous member with continuous open pores and disposed in the housing 2 such that it partitions the interior of the housing 2 into a blood inlet portion 3a and a blood outlet portion 3b. As shown in Fig. 3, the filter 6 of the present invention is received in the housing 2 such that blood, etc. introduced into the housing 2 through the blood inlet 2a cannot exit from the blood outlet 2b without passing through the filter 6. A circumferential portion of the filter 6 is water-tightly disposed between inner and outer two members of the housing 2. The filter 6, as shown in Fig. 3, is partly clamped by a plurality of projections 2c formed on the inner surface of the two constituent members of the housing 2 to prevent deformation of the filter during operation and to

be usable for the housing 2 are various materials such as polycarbonates, acrylic resins, polyethylene terephthalate, polyethylene, polypropylene, polystyrene, polyvinyl chloride resins, acryl-styrene copolymers, acryl-butylene-styrene copolymers, and the like. Particularly preferable are polycarbonates, acrylic resins, polyethylene terephthalate, polyethylene, polypropylene, polysiloxane, and polyvinyl chloride resins. The inner surface of the housing 2 is preferably treated to have a hydrophilic nature to allow adhesion of blood cells thereto. Suitable hydrophilic treatment is coating or bonding of a hydrophilic substance, or a surface treatment such as plasma treatment, corona treatment, etc.

In the leukocyte remover 1 according to one embodiment of the present invention shown in Fig. 3, a pre-filter portion (the right side portion of the filter 6 in Fig. 3) on the upstream side of a main filter portion (the left side portion of the filter 6 in Fig. 3) functions to remove fine particles in the blood (for example, gels, microaggregates, etc.) and huge leukocyte particles and leukocytes from the blood, before introducing the blood into the main filter portion to prevent clogging of the main filter portion.

A suitable porous member used for the pre-filter portion is a three-dimensionally reticular, porous member with continuous open pores having a most frequent pore diameter of about 2 μm to about 4 μm , an average pore diameter ratio of 2.0 to 2.5, and a thickness of about 0.3 mm to about 1.5 mm. A suitable number of such porous members laminated is 1 to 5. A suitable porous member used for the main filter portion is a three-dimensionally reticular, porous member with continuous open pores having a most frequent pore diameter of about 1 μm to about 3 μm and smaller than that of the pre-filter portion, an average pore diameter ratio of 1.5 to 2.0, and a thickness of about 0.3 mm to about 1.5 mm. A suitable number of such porous members laminated is 1 to 5.

In a preferred embodiment, the pre-filter portion may be made by stacking two porous polyurethane films each having a most frequent pore diameter of 2.5 μm to 3.5 μm , an average pore diameter ratio of 2.5, and a thickness of about 0.6 mm, and treated by a surfactant, and the main filter portion may be made by stacking four porous polyurethane members each having a most frequent pore diameter of 1.0 μm to 2.0 μm , an average pore diameter ratio of 1.7, and a thickness of about 0.6 mm, and treated by a surfactant.

The filter may be a single-layered member in lieu of the laminate stated above. The thinner the filter, the easier it is to make the integral structure uniform, and the easier the fabrication of a filter meeting the desired numerical conditions. Further, taking into intended use, sheet areas and other factors into consideration, any appropriate number of sheets may be laminated to make the desired leukocyte remover. The number of porous sheets laminated may appropriately be determined by considering the flow rate, filtration time, likelihood of clogging, etc.

Any surfactant may be used for a hydrophilic treatment, and suitably usable are, for example, glycerol monolaurate, and polyether-type surfactants (for example, Pluronic surfactant). Instead of using a surfactant, the porous member may be hydrophilic-treated (for example, plasma-treated).

An example of usage of the leukocyte-separating filter 6 of the present invention will be explained below with reference to Fig. 7 showing a circuit for removing leukocytes from a blood preparation such as platelet concentrate which does not contain cells for component transfusion of platelets to a patient.

The separation of leukocytes with the circuit of Fig. 7 is started by closing clamps 20a, 20b. Protectors 21a, 21b are then removed, and needles 22a, 22b are attached to a bag (not shown) of a blood preparation (specifically, platelet concentrate) and a rinse bag (not shown). The blood preparation bag and the rinse bag are hung down from an irrigator (not shown).

While maintaining the leukocyte remover 1 upside down, the clamps 20a and a roller clamp 23 are opened for priming the leukocyte remover 1. After the priming of the leukocyte remover 1 is completed, the leukocyte remover 1 is returned to its original posture. After that, by making an instillator 24 upside down, the blood preparation is introduced into the instillator 24. After the blood preparation occupies about a half volume of the instillator 24, the instillator 24 is returned to the original posture. When the blood preparation reaches a tip end of a lock connector 25, the roller clamp 23 is closed.

With a syringe needle attached to the end of the lock connector 25, instillation (component transfusion, i.e. platelet transfusion in this case) into the vein of a patient is started. The flow rate of instillation is adjusted by the roller clamp 23.

When the blood preparation bag is emptied, the roller clamp 23 is closed and the clamp 20b is opened to introduce a rinse into the blood preparation bag. When 100 ml or so of the rinse is introduced, the clamp 20b is closed and the roller clamp 23 is opened to resume the component transfusion. When the rinse in the blood preparation bag is exhausted, the rinse in the instillator tube 27 is recovered by opening an air vent 26, and the transfusion is finished.

Another example of usage of the leukocyte-separating filter 6 of the present invention will be explained below with reference to Fig. 8. The circuit of Fig. 8 uses the leukocyte-separating filter 6 of the present invention to remove leukocytes and recover platelets from a blood preparation not including red cells, such as a platelet concentrate. The separation of leukocytes by the circuit is substantially the same as that explained above, except for differences in that transfusion using the rinse is conducted and that the remover 1 does not include the air vent 12d whose function in the process stated above is performed by an air vent 37a. Incidentally, transfusion using a rinse may not be conducted in the circuit comprising leukocyte remover 1, and the leukocyte remover 1 may have the air vent 12d.

[4] Leukocyte/platelet remover

A leukocyte/platelet-separating filter and a leukocyte/platelet remover comprising the leukocyte/platelet-separating filter according to the present invention will be explained below with reference to the drawings. Fig. 4 is a front elevation showing an example of the leukocyte/platelet remover comprising the leukocyte/platelet-separating filter according to the present invention. Fig. 5 is a right side elevational view of Fig. 4. Fig. 6 is a cross-sectional view taken along the B-B line in Fig. 4.

The leukocyte/platelet remover 10 comprising the leukocyte/platelet-separating filter 16 of the present invention includes housing 12 having a blood inlet 12a and a blood outlet 12b, and the leukocyte/platelet-separating filter 16 disposed in the housing 12 such that it partitions the interior of the housing 12 into a blood inlet portion 13a and a blood outlet portion 13b. The leukocyte/platelet-separating filter 16 is composed of a pre-filter 16a for removing microaggregates and gels occurring in blood, and a platelet-adsorbing, three-dimensionally reticular, porous member with continuous open pores (main filter) 16b having a most frequent pore diameter of 1 μm to 5 μm and a ratio of a weight-average pore diameter to a number-average pore diameter in the range of 1.5 to 2.5. With this structure, the main filter 16b exhibits a good ability to capture both leukocytes and platelets.

The pre-filter 16a is preferably composed of non-woven fabrics in the form of a flat sheet each having a weight/area value of 10 g/m^2 to 80 g/m^2 , an average fiber diameter of 10 μm to 20 μm and a thickness of about 0.3 mm to about 0.6 mm. Two to five such nonwoven fabrics are preferably laminated. The main filter portion is preferably composed of a primary main filter portion having a wider pore diameter distribution and a secondary main filter portion having a narrower pore diameter distribution. The primary main filter portion is preferably composed of three-dimensionally reticular, porous members with continuous open pores each having a most frequent pore diameter of about 2 μm to about 3 μm , an average pore diameter ratio of 1.8 to 2.5 and a thickness of about 0.5 mm to about 2 mm. Two to five such porous members are preferably laminated. The secondary main filter portion is preferably composed of three-dimensionally reticular, porous members with continuous open pores each having a most frequent pore diameter of about 2 μm to about 3 μm , an average pore diameter ratio of 1.5 to 2.1 and a thickness of about 0.2 mm to about 2 mm. Two to five such porous members are preferably laminated. The porous members used for the secondary main filter portion may be the same as those used for the primary main filter portion.

In a preferred example, the pre-filter 16a is made by stacking three sheets of non-woven polyester fabrics each having an average fiber diameter of 12 μm and a bulk density of 0.1875 g/cm^3 or so to a thickness of about 0.1 mm. An upstream portion of the main filter 16b (the right side portion of the main filter 16b in Fig. 6) constitutes a primary main filter portion made by stacking on a 0.2-mm-thick sheet of non-woven polyester fabrics as a support member three surfactant-treated, polyurethane films each having a most frequent pore diameter of 1.0 μm to 3.0 μm , an average pore diameter ratio of 1.5 and a thickness of about 1.0 mm. A downstream portion of the main filter 16b (the left side portion of the main filter 16b in Fig. 6) constitutes a secondary main filter portion made by stacking three porous polyurethane films identical to those of the upstream portion but subjected to a cationic treatment and a surfactant treatment. Thus, the leukocyte/platelet-separating filter of the present invention is preferably made by laminating a plurality of such porous members. The number of porous sheets stacked may be appropriately determined, considering such factors as removal rate, filtration time and likelihood of clog.

Any surfactants may be used for a hydrophilic treatment, and suitable surfactants are, for example, deca-glycerol monol and polyether-type surfactants (for example, Pluronic surfactant). Instead of using a surfactant, the porous member may be subjected to a hydrophilic treatment (for example, plasma treatment).

The pre-filter 16a is used to remove microaggregates and gels originally contained in the blood or generated in the blood aggregation during storage. The porous member constituting the primary main filter portion disposed on the upstream side functions to remove leukocytes having larger diameters than its own pore diameters. Negative-charged platelets have smaller diameters than those of the porous member constituting the secondary main filter portion disposed on the downstream side. Nevertheless, since the porous member of the secondary main filter portion is positive-charged by a cationic treatment, platelets are electrically trapped by the porous member. Leukocytes passing through the primary main filter portion, although very small, are also removed by the secondary main filter portion. Also, red cells having larger diameters than the pore diameters of the porous members constituting the primary and secondary main filter portions can pass through the main filter 16b, because they are easily deformable.

Reasons why the porous member of the main filter 16b is combined with the non-woven fabrics are, among others, that the nonwoven fabrics having little anti-thrombogenic nature function to adsorb highly adherent platelets, that a step for stripping them in the sheet fabricating process can be omitted, that the porous member can be more easily mounted in the housing because the non-woven fabrics keep the porous member in a proper shape.

As shown in Fig. 6, the housing 12 of the leukocyte/platelet remover 10 has an air vent 12d near an upper portion. The air vent 12d facilitates the removal of an air in the course of priming the remover 10, the operation of starting or stopping filtration, recovery of residual liquids in the remover, the removal of an air from the recovery bag, and so forth. Although the air vent 12d used in this embodiment can be opened and closed by a cap, it may be configured otherwise.

An example of usage of the leukocyte/platelet-separating filter 16 according to the present invention will be explained with reference to Fig. 9. The leukocyte/platelet remover 10 with the leukocyte/platelet-separating filter 16 according to the present invention is connected in a circuit as shown, for example, in Fig. 9. The circuit shown in Fig. 9 is for use in component transfusion of red cells to a patient while removing leukocytes and platelets from a whole blood or a blood preparation in which red cells (for example, concentrated red cells) are separated by using the leukocyte/platelet remover 10 including the leukocyte/platelet-separating filter 16 according to the present invention.

The process of separation of leukocytes and platelets by this circuit is the same as those stated above, except that transfusion operation by a rinse is not performed, and that the air vent 12d of the remover 10 is opened to transfuse red cells remaining in the tube on the outlet side to a patient after the blood preparation bag is emptied. The circuit comprising the leukocyte/platelet remover 10 may also be used for transfusing operation by a rinse, and the leukocyte/platelet remover 10 may not necessarily have the air vent 12d.

Another example of usage of the leukocyte/platelet-separating filter 16 of the present invention will be explained with reference to Fig. 10. The circuit shown in Fig. 10 is intended to remove leukocytes and platelets and recover red cells from a whole blood or blood preparations including red cells by using the leukocyte/platelet remover 10 comprising the leukocyte/platelet-separating filter 16.

The process of separation of leukocytes by this circuit is conducted by opening a peel tab 30 and attaching a needle 33 to a recovery bag 32 to a vent 31, closing clamps 34a, 34b and a cap 14 of the air vent 12d, removing a protector 35, attaching a needle 36 to a blood preparation bag (not shown), and hanging it down from an irrigator (not shown).

The clamps 34a and the cap 14 of the air vent 12d are then opened for priming the remover 10. When the blood preparation reaches the air vent 12d, the air vent 12d is closed by the cap 14, and the clamp 34b is opened, thereby starting filtration.

When the blood preparation bag is emptied, a residual blood preparation on the inlet side is recovered by opening the air vent 37, and a residual blood preparation on the outlet side is recovered by opening the cap 14 of the air vent 12d. The residual blood preparation in the tube 38 on the outlet side is recovered in the bag 32 by squeezing the tube 38 with roller pincers. If the need for removal of an air from the recovery bag 32, the air can be expelled from the recovery bag 32 through the air vent 37 by moving the air toward the tube 38 and then pressing the recovery bag 32. Sealing the tube 38, the recovery bag 32 is disconnected from the circuit to finish the process of separating leukocytes and platelets.

The present invention will be explained in greater detail by way of Examples below without intention of limiting the pre invention thereto.

Examples 1-6, Comparative Examples 1-4

Leukocyte/platelet-separating filters having the construction shown in Fig. 4 were made by using porous polyvinyl formal members having a thickness of 1.3 mm, a filtration area of 50 cm², and most frequent pore diameters and average pore diameter ratios shown in Table 1. Since the porous polyvinyl formal members are hydrophilic and platelet-adsorbing, they were not subjected to any particular hydrophilic treatment and cationic treatment.

Every two of the porous members shown in Table 1 were stacked to make a leukocyte/platelet-separating filter, which was assembled in a leukocyte/platelet remover as shown in Fig. 6. Each of such leukocyte/platelet removers was mounted to a circuit having the structure shown in Fig. 10. 0.5 units of CPD-added concentrated red cells (CRC) obtained from 400 ml human blood were caused to flow through the separating filter gravitationally.

The numbers of blood cells in CRC before and after the treatment, and the numbers of red cells and platelets after the treatment were measured with an automatic blood cell counter (Sysmex NE-6000 produced by Toa Medical Electronics Co., Ltd.). The total numbers of respective blood cell components were measured on a liquid volume basis, and the red cell recovery rate and the platelet removal rates were determined.

The numbers of leukocytes after the treatment were measured with a flow cytometer (Cyto-ACE 150 produced by Nippon Bunko K. K.) and a Nageotte hemocytometer. The total number of leukocytes was measured on a liquid volume basis, and the removal rate of leukocytes was determined. The results are shown in Table 2.

Age	Sex	Rate
15-19	Male	0.000
15-19	Female	0.000
20-24	Male	0.000
20-24	Female	0.000
25-29	Male	0.000
25-29	Female	0.000
30-34	Male	0.000
30-34	Female	0.000
35-39	Male	0.000
35-39	Female	0.000
40-44	Male	0.000
40-44	Female	0.000
45-49	Male	0.000
45-49	Female	0.000
50-54	Male	0.000
50-54	Female	0.000
55-59	Male	0.000
55-59	Female	0.000
60-64	Male	0.000
60-64	Female	0.000
65-69	Male	0.000
65-69	Female	0.000
70-74	Male	0.000
70-74	Female	0.000
75-79	Male	0.000
75-79	Female	0.000
80-84	Male	0.000
80-84	Female	0.000
85-89	Male	0.000
85-89	Female	0.000
90-94	Male	0.000
90-94	Female	0.000
95-99	Male	0.000
95-99	Female	0.000

<tb>Head Col 1:

<tb>Head Col 2 to 3: Porous Member

<tb>SubHead Col 1: No.

SubHead Col 1: Most Frequent Pore Diameter (μm)	SubHead Col 2: Most Frequent Pore Diameter (μm)
100	100
200	200
300	300
400	400
500	500
600	600
700	700
800	800
900	900
1000	1000
1100	1100
1200	1200
1300	1300
1400	1400
1500	1500
1600	1600
1700	1700
1800	1800
1900	1900
2000	2000
2100	2100
2200	2200
2300	2300
2400	2400
2500	2500
2600	2600
2700	2700
2800	2800
2900	2900
3000	3000
3100	3100
3200	3200
3300	3300
3400	3400
3500	3500
3600	3600
3700	3700
3800	3800
3900	3900
4000	4000
4100	4100
4200	4200
4300	4300
4400	4400
4500	4500
4600	4600
4700	4700
4800	4800
4900	4900
5000	5000
5100	5100
5200	5200
5300	5300
5400	5400
5500	5500
5600	5600
5700	5700
5800	5800
5900	5900
6000	6000
6100	6100
6200	6200
6300	6300
6400	6400
6500	6500
6600	6600
6700	6700
6800	6800
6900	6900
7000	7000
7100	7100
7200	7200
7300	7300
7400	7400
7500	7500
7600	7600
7700	7700
7800	7800
7900	7900
8000	8000
8100	8100
8200	8200
8300	8300
8400	8400
8500	8500
8600	8600
8700	8700
8800	8800
8900	8900
9000	9000
9100	9100
9200	9200
9300	9300
9400	9400
9500	9500
9600	9600
9700	9700
9800	9800
9900	9900
10000	10000

	<tb>SubHead Col 3: Average Pore Diameter Ratio <SEP>Example 1<SEP>1.0<SEP>2.0
--	---

<tb><SEP>Example 2<SEP>2.0<SEP>1.9

<tb><SEP>Example 3<SEP>3.5<SEP>1.8

<tb><SEP>Example 4<SEP>4.0<SEP>1.7

<tb><SEP>Example 5<SEP>4.5<SEP>2.5

<tb><SEP>Example 6<SEP>5.0<SEP>2.0

<tb><SEP>Com. Ex. 1<SEP>0.5<SEP>2.1

<tb><SEP>Com. Ex. 2<SEP>2.0<SEP>1.4

<tb><SEP>Com. Ex. 3<SEP>6.0<SEP>1.4

<tb><SEP>Com. Ex. 4<SEP>6.0<SEP>2.0

<tb></TABLE>

Year	2000	2001	2002	2003	2004
1	10	15	20	25	30
2	20	25	30	35	40
3	30	35	40	45	50
4	40	45	50	55	60
5	50	55	60	65	70

Head Col 1:	Head Col 2:	Head Col 3:	Head Col 4:	Head Col 5:	Head Col 6:	Head Col 7:	Head Col 8:	Head Col 9:	Head Col 10:	Head Col 11:	Head Col 12:	Head Col 13:	Head Col 14:	Head Col 15:	Head Col 16:	Head Col 17:	Head Col 18:	Head Col 19:	Head Col 20:	Head Col 21:	Head Col 22:	Head Col 23:	Head Col 24:	Head Col 25:	Head Col 26:	Head Col 27:	Head Col 28:	Head Col 29:	Head Col 30:	Head Col 31:	Head Col 32:	Head Col 33:	Head Col 34:	Head Col 35:	Head Col 36:	Head Col 37:	Head Col 38:	Head Col 39:	Head Col 40:	Head Col 41:	Head Col 42:	Head Col 43:	Head Col 44:	Head Col 45:	Head Col 46:	Head Col 47:	Head Col 48:	Head Col 49:	Head Col 50:	Head Col 51:	Head Col 52:	Head Col 53:	Head Col 54:	Head Col 55:	Head Col 56:	Head Col 57:	Head Col 58:	Head Col 59:	Head Col 60:	Head Col 61:	Head Col 62:	Head Col 63:	Head Col 64:	Head Col 65:	Head Col 66:	Head Col 67:	Head Col 68:	Head Col 69:	Head Col 70:	Head Col 71:	Head Col 72:	Head Col 73:	Head Col 74:	Head Col 75:	Head Col 76:	Head Col 77:	Head Col 78:	Head Col 79:	Head Col 80:	Head Col 81:	Head Col 82:	Head Col 83:	Head Col 84:	Head Col 85:	Head Col 86:	Head Col 87:	Head Col 88:	Head Col 89:	Head Col 90:	Head Col 91:	Head Col 92:	Head Col 93:	Head Col 94:	Head Col 95:	Head Col 96:	Head Col 97:	Head Col 98:	Head Col 99:	Head Col 100:
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80	81	82	83	84	85	86	87	88	89	90	91	92	93	94	95	96	97	98	99	100

<tb>Head Col 2 to 5: Separation Results

[illegible]

SubHead Col 1: Filtering Time (minute)	SubHead Col 2: Filtering Time (minute)
1	1
2	2
3	3
4	4
5	5
6	6
7	7
8	8
9	9
10	10
11	11
12	12
13	13
14	14
15	15
16	16
17	17
18	18
19	19
20	20
21	21
22	22
23	23
24	24
25	25
26	26
27	27
28	28
29	29
30	30
31	31
32	32
33	33
34	34
35	35
36	36
37	37
38	38
39	39
40	40
41	41
42	42
43	43
44	44
45	45
46	46
47	47
48	48
49	49
50	50
51	51
52	52
53	53
54	54
55	55
56	56
57	57
58	58
59	59
60	60
61	61
62	62
63	63
64	64
65	65
66	66
67	67
68	68
69	69
70	70
71	71
72	72
73	73
74	74
75	75
76	76
77	77
78	78
79	79
80	80
81	81
82	82
83	83
84	84
85	85
86	86
87	87
88	88
89	89
90	90
91	91
92	92
93	93
94	94
95	95
96	96
97	97
98	98
99	99
100	100

SubHead Col 1: Leukocyte Removal Rate (%)	SubHead Col 2: Leukocyte Removal Rate (%)	SubHead Col 3: Leukocyte Removal Rate (%)
1	2	3
4	5	6
7	8	9
10	11	12
13	14	15
16	17	18
19	20	21
22	23	24
25	26	27
28	29	30
31	32	33
34	35	36
37	38	39
40	41	42
43	44	45
46	47	48
49	50	51
52	53	54
55	56	57
58	59	60
61	62	63
64	65	66
67	68	69
70	71	72
73	74	75
76	77	78
79	80	81
82	83	84
85	86	87
88	89	90
91	92	93
94	95	96
97	98	99
100	101	102
103	104	105
106	107	108
109	110	111
112	113	114
115	116	117
118	119	120
121	122	123
124	125	126
127	128	129
130	131	132
133	134	135
136	137	138
139	140	141
142	143	144
145	146	147
148	149	150
151	152	153
154	155	156
157	158	159
160	161	162
163	164	165
166	167	168
169	170	171
172	173	174
175	176	177
178	179	180
181	182	183
184	185	186
187	188	189
190	191	192
193	194	195
196	197	198
199	200	201
202	203	204
205	206	207
208	209	210
211	212	213
214	215	216
217	218	219
220	221	222
223	224	225
226	227	228
229	230	231
232	233	234
235	236	237
238	239	240
241	242	243
244	245	246
247	248	249
250	251	252
253	254	255
256	257	258
259	260	261
262	263	264
265	266	267
268	269	270
271	272	273
274	275	276
277	278	279
280	281	282
283	284	285
286	287	288
289	290	291
292	293	294
295	296	297
298	299	300
301	302	303
304	305	306
307	308	309
310	311	312
313	314	315
316	317	318
319	320	321
322	323	324
325	326	327
328	329	330
331	332	333
334	335	336
337	338	339
340	341	342
343	344	345
346	347	348
349	350	351
352	353	354
355	356	357
358	359	360
361	362	363
364		

SubHead Col 1: Red Cell Recovery Rate (%)	SubHead Col 2: Red Cell Recovery Rate (%)	SubHead Col 3: Red Cell Recovery Rate (%)	SubHead Col 4: Red Cell Recovery Rate (%)
1	2	3	4
5	6	7	8
9	10	11	12
13	14	15	16
17	18	19	20
21	22	23	24
25	26	27	28
29	30	31	32
33	34	35	36
37	38	39	40
41	42	43	44
45	46	47	48
49	50	51	52
53	54	55	56
57	58	59	60
61	62	63	64
65	66	67	68
69	70	71	72
73	74	75	76
77	78	79	80
81	82	83	84
85	86	87	88
89	90	91	92
93	94	95	96
97	98	99	100

<tb>SubHead Col 5: Platelet Removal Rate (%)	<SEP>	Example 1	<SEP>	14	<SEP>	99.9	<SEP>	97	<SEP>	92
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<tb><SEP>Example 2<SEP>12<SEP>99.9<SEP>97<SEP>92

<tb><SEP>Example 3<SEP>11<SEP>99.9<SEP>97<SEP>91

<tb><SEP>Example 4<SEP>10<SEP>99.9<SEP>97<SEP>91

<tb><SEP>Example 5<SEP>8<SEP>99.5<SEP>98<SEP>90

<tb><SEP>Example 6<SEP>10<SEP>99.7<SEP>98<SEP>90

<tb><SEP>Com. Ex. 1<SEP>53<SEP>99.9<SEP>94<SEP>93

<tb><SEP>Com. Ex. 2<SEP>47<SEP>99.9<SEP>92<SEP>92

<tb><SEP>Com. Ex. 3<SEP>6<SEP>93.2<SEP>99<SEP>82

<tb><SEP>Com. Ex. 4<SEP>5<SEP>91.0<SEP>99<SEP>77

<tb></TABLE>

Table 2 proves that the leukocyte/platelet-separating filters of Examples 1 to 6 composed of porous members having more frequent pore diameters in the range of 1 μm to 5 μm and average pore diameter ratios in the range of 1.5 to 2.5 exhibit good leukocyte removal rates in a practical period of time, and that their red cell recovery rates and platelet removal rates are better than those of Comparative Examples 1 to 4.

The same experiment was conducted with porous polyurethane members having a porosity of about 87%, a thickness of a filtration area of 50 cm², and most frequent pore diameters and average pore diameter ratios shown in Table 1. As a substantially the same results were obtained. Incidentally, a primary filter portion of the leukocyte/platelet-separating filter produced by stacking three porous polyurethane members subjected to a hydrophilic treatment with glycerol monolaurate (decaglycerin monolaurate). A secondary filter portion of the leukocyte/platelet-separating filter was produced by using same porous members as in the primary filter portion, by subjecting them to a plasma treatment, graft copolymerization of glycidyl methacrylate, fixing of a cationic agent (Cationon UK produced by Ipposha Oil & Fat Industries K.K.) and then treatment with glycerol monolaurate, and by stacking three of them. The housing used was configured as shown in Figs. The housing contained the separating filter to form the leukocyte/platelet remover as shown in Fig. 6.

Examples 7-10, Comparative Examples 5-7

A leukocyte/platelet-separating filter shown in Fig. 11 was made by using porous polyurethane members having a thickness of 0.6 mm, a filtration area of 3 cm², a porosity of about 87%, and most frequent pore diameters and average pore diameter ratios shown in Table 3. The filter included a pre-filter portion made by stacking two such porous members shown in Fig. 11 subjected to a hydrophilic treatment with glycerol monolaurate, and a main filter portion made by stacking four such porous members treated by glycerol monolaurate like those of the pre-filter portion. The housing used was configured as shown in Fig. 11, and contained the above separating filter to form a leukocyte remover.

The leukocyte-separating filters of Examples 7 to 10 and Comparative Examples 5 to 7 were incorporated into circuits having the construction shown in Fig. 11 to form experimental circuits. Lymphocyte-containing, platelet-rich plasma (PRP) (platelets: $3.5 \times 10^5 / \mu\text{l}$ - $5.5 \times 10^5 / \mu\text{l}$, and leukocytes: $3.5 \times 10^3 / \mu\text{l}$ - $4.5 \times 10^3 / \mu\text{l}$) was prepared by adding separated lymphocytes by a density-gradient centrifugal separation method to a platelet-rich plasma (PRP) collected from added fresh blood of healthy humans. The experiment was conducted by passing the lymphocyte-containing PRP through experimental circuits shown in Fig. 11 at a flow rate of 1 ml/minute.

The numbers of platelets in PRP before and after the treatment and the numbers of leukocytes in PRP before the treatment were measured with an automatic blood cell counter (Sysmex NE-6000 produced by Toa Medical Electronics Co., Ltd.), and the number of leukocytes after the treatment was measured with a flow cytometer (Cyto-ACE 150 produced by Nippon Bun K.) and a Nageotte hemocytometer. The total numbers of respective blood cell components were measured on a liquid volume basis, and the leukocyte removal rates and the platelet recovery rates were calculated therefrom. The results are shown in Table 4.

Table 3 Columns=5				
Head Col 1:				
Head Col 2 to 5: Porous Member				
SubHead Col 1>:				
SubHead Col 2 to 3: Pre-filter Portion				
SubHead Col 4 to 5: Main Filter Portion				
SubHead Col 1: No.				
SubHead Col 2: Most Frequent Pore Diameter				
SubHead Col 3: Average Pore Diameter Ratio				
SubHead Col 4: Most Frequent Pore Diameter				
SubHead Col 5: Average Pore Diameter Ratio				
Example 7	3.5 μm	1.8	2.0 μm	2.0
Example 8	3.5 μm	1.8	2.0 μm	1.9
Example 9	4.0 μm	1.7	2.0 μm	1.9
Example 10	4.5 μm	2.5	1.0 μm	2.0
Com. Ex. 5	5.0 μm	2.0	1.0 μm	2.0
Com. Ex. 6	6.0 μm	2.0	0.5 μm	2.1
Com. Ex. 7	6.0 μm	2.0	2.0 μm	1.4

Table 4 proves that the leukocyte filters of Examples 7 to 10 composed of porous members having most frequent pore diameters in the range of 1 μm to 5 μm and average pore diameter ratios in the range of 1.5 to 2.5 exhibited better leukocyte removal rates and platelet removal rates than those of Comparative Examples 5 to 7.

As explained above, since the leukocyte-separating filters of the present invention are composed of three-dimensionally reticular, porous member with continuous open pores having most frequent pore diameters ranging from 1 μm to 5 μm , they exhibit high and stable abilities to capture leukocytes. Thus, leukocytes contained in the blood are efficiently and quickly captured when passing through complicated flow paths of continuous open pores in the matrix of the porous member. By meeting the requirement that the ratio of a weight-average pore diameter to a number-average pore diameter is in the range of 1.5 to 2.5, the leukocyte removal rate is further improved. Since the flow path of the filter is defined by the three-dimensionally reticular, continuous texture of a porous member (continuous open pores defined by the matrix of the porous member), the

is stable and uniform in performance. The filter also suffers from substantially no outflow of foreign matters from the porous members and channeling of the flow paths during operation. Moreover, since the flow paths of the filter are formed at the time of production of the porous member, the filter can very easily be fabricated.

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Claims of corresponding document: EP0630675

1. A leukocyte-separating filter composed of a three-dimensionally reticular, porous member with continuous open pores having a most frequent pore diameter in the range of 1 μ m to 5 μ m and a ratio of weight-average pore diameter to number-average pore diameter in the range of 1.5 to 2.5.
2. The leukocyte-separating filter according to claim 1, wherein said porous member does not adsorb platelets.
3. The leukocyte-separating filter according to claim 2, wherein said filter is composed of a plurality of said three-dimensionally reticular, porous members with continuous open pores, and wherein one or more of said porous members located on the upstream side are larger in a ratio of weight-average pore diameter to number-average pore diameter than the remaining members located on the downstream side.
4. A leukocyte/platelet-separating filter comprising a platelet-adsorbing, three-dimensionally reticular, porous member with continuous open pores having a most frequent pore diameter in the range of 1 μ m to 5 μ m and a ratio of weight-average pore diameter to number-average pore diameter in the range of 1.5 to 2.5.
5. A leukocyte/platelet-separating filter comprising a laminate of at least one platelet-nonadsorbing, three-dimensionally reticular, porous member with continuous open pores having a most frequent pore diameter in the range of 1 μ m to 5 μ m and a ratio of weight-average pore diameter to number-average pore diameter in the range of 1.5 to 2.5, and at least one platelet-adsorbing, three-dimensionally reticular, porous member with continuous open pores having a most frequent pore diameter in the range of 1 μ m to 5 μ m and a ratio of weight-average pore diameter to number-average pore diameter in the range of 1.5 to 2.5.
6. The leukocyte/platelet-separating filter according to claim 5, wherein said platelet-nonadsorbing porous member is located on the upstream side and said platelet-adsorbing porous member is located on the downstream side.
7. The leukocyte/platelet-separating filter according to claim 6, wherein said porous member located on the upstream side is larger in a ratio of weight-average pore diameter to number-average pore diameter than said porous member located on the downstream side.
8. The leukocyte/platelet-separating filter according to claim 5, wherein said platelet-adsorbing porous member is located on the upstream side and said platelet-nonadsorbing porous member is located on the downstream side.
9. The leukocyte/platelet-separating filter according to claim 8, wherein said porous member located on the upstream side has a larger ratio of weight-average pore diameter to number-average pore diameter, and said porous member located on the downstream side has a smaller ratio of weight-average pore diameter to number-average pore diameter.
10. The leukocyte/platelet-separating filter according to claim 5, wherein said platelet-nonadsorbing porous member is located on the upstream side and has a smaller ratio of weight-average pore diameter to number-average pore diameter, and said platelet-adsorbing porous member is located on the downstream side and has a larger ratio of weight-average pore diameter to number-average pore diameter.
11. A leukocyte remover comprising a housing having a blood inlet and a blood outlet; and a leukocyte-separating filter disposed in said housing such that it partitions the interior of the housing into a blood inlet portion and a blood outlet portion.
12. A leukocyte/platelet remover comprising a housing having a blood inlet and a blood outlet; and a leukocyte/platelet-separating filter disposed in said housing such that it partitions the interior of the housing into a blood inlet portion and a blood outlet portion.

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